

Applicant: Braud et al.  
Application No.: 09/555,555

### IN THE SPECIFICATION

Please replace the paragraph beginning at page 13, line 28, with the following rewritten paragraph:

HLA-E for use in the invention which is present at surface of a cell on the other hand is preferably, although not necessarily, a membrane-bound form of HLA-E containing a transmembrane domain. It may or not also have a cytoplasmic domain. In order to get HLA-E expressed at the surface of a cell which does not normally express HLA-E at its surface, it is necessary to provide a peptide which binds in the HLA-E peptide binding groove. The peptide may be derived either from an HLA leader sequence which is permissive for HLA-E expression, or it may be derived from another source which expresses peptides that bind to HLA-E and induce its expression. Such other sources include viruses which escape NK cell-mediated cytotoxicity by encoding a peptide which binds to HLA-E and induces its expression. For example, the human cytomegalovirus (HCMV) encodes a protein known as UL40 (Accession No. p16780) which possess a peptide (VMAPRTLIL) capable of binding to HLA-E (see fourth leader sequence peptide listed in Table 1).<sup>4</sup>

Please replace the paragraph beginning at page 20, line 4, with the following rewritten paragraph:

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C<sup>3</sup> 4 HLA-E tetrameric complexes were constructed by refolding recombinant HLA-E and  $\beta$ 2m molecules *in vitro* with a synthetic peptide (VMAPRTVLL) [SEQ ID NO 3] derived from residues 3-11 of the signal sequence of HLA-B\*0801. A biotinylation site was engineered in the C terminus of the HLA-E heavy chain, allowing HLA-E/  $\beta$ 2m/peptide complexes to be enzymatically biotinylated using *E.coli* BirA enzyme and conjugated with phycoerthrin (PE)-labeled Extravidin to create tetrameric complexes. HLA-A and -B tetrameric complexes have proved to be very efficient at specifically binding to T cell receptors on antigen-specific CD8\* T cells from peripheral blood *in vitro* (Altman et al 1996 *Science* 274: 94-96). -

Please replace the paragraph beginning at page 21, line 1, with the following rewritten paragraph:

C<sup>4</sup> 4 HLA-E tetrameric complexes were generated essentially as described (Altman et al 1996). Briefly, HLA-E and  $\beta$ 2m proteins were over-expressed in *E.coli* strains BL21 (DE3) pLysS and XA90 respectively, purified from inclusion bodies, solubilised into a urea solution, then refolded by dilution *in vitro* with a synthetic peptide (VMAPRTVLL) [SEQ ID NO 3] from HLA-B\*0801 leader sequence (Research Genetics). HLA-E heavy chain/ $\beta$ 2m/peptide complexes were biotinylated with BirA enzyme, purified by FPLC and Mono-Q ion exchange chromatography, then complexed in a 4:1 molar ratio with Extravidin-PE (Sigma). ↓